DPP General Description

About 16 million people in the United States have impaired glucose tolerance (IGT), in which muscle, fat, and liver cells fail to use insulin effectively. Although people with IGT are not yet diabetic, IGT is a precursor to non-insulin-dependent diabetes mellitus (NIDDM). The pancreas compensates for IGT by producing more insulin, and the insulin response becomes abnormal. IGT causes elevated blood glucose levels and can be as diagnosed by an oral glucose tolerance test (OGT). Between 1% and 10% of people with IGT will develop diabetes per year, and risk factors include obesity, a sedentary lifestyle, a family history of diabetes, and ethnicity. DPP subjects were overweight and had IGT, and about 10% of the subjects in the placebo group developed diabetes per year. The DPP compared the effectiveness of a life style and pharmacological interventions in different age groups and ethnicities.

The principal objective of the Diabetes Prevention Program (DPP) was to prevent or delay the development of non-insulin dependent diabetes mellitus (NIDDM) using pharmacological or lifestyle interventions in high-risk adults. The DPP was a randomized clinical trial with three treatment arms for the prevention of NIDDM in high-risk adults with impaired glucose tolerance (IGT), which is a risk factor for the development of NIDDM. The pharmacological interventions were double blinded and placebo controlled.

Volunteers were recruited from populations at high risk for impaired glucose tolerance and NIDDM, including persons with a family history of NIDDM, the elderly, overweight individuals, women with a history of gestational diabetes, and minority populations including African Americans, Hispanic Americans, Asian and Pacific Island Americans, and Native Americans. To be eligible, persons older than 25 years had to demonstrate IGT with plasma glucose levels 95-125 mg/dL (5.3-6.9 mmol/L) fasting and 140- 199 mg/dL (7.8 - 11.0 mmol/L) two hours after a 75 gram oral glucose tolerance test (OGTT). The study-wide goal was that approximately 50% of the study population be composed of minorities and approximately 20% be 65 years of age or older.

The interventions included an intensive lifestyle intervention and two pharmacological interventions. The intensive lifestyle intervention focused on a healthy diet to achieve and maintain at least a 7% loss of body weight and at least 150 min/week of moderate intensity exercise. Standard lifestyle recommendations, which included conventional instructions regarding diet and exercise, were provided to all participants, including a placebo treated group which served as the control group for the study. The pharmacological interventions included the biguanide metformin and the thiazolidinedione troglitazone. Randomization to the troglitazone pharmacological intervention was suspended on May 27, 1998, and discontinued by the NIDDK on June 3, 1998 because of liver toxicity.

The primary outcome was the development of diabetes, defined as fasting plasma glucose level > 126 mg/dL (7.0 mmol/L), or two 75 gram OGTT resulting in 2-hour plasma

glucose > 200 mg/dL (11.1 mmol/L). Secondary outcomes included changes in glycemia, insulin secretion and sensitivity, obesity, physical activity and nutrient intake, quality of life, adverse events, and cardiovascular disease and its risk factors.

Randomization into the DPP began in July 1996 and continued nearly 3 years until May 1999, and the study was terminated in June 2003. Participants were seen quarterly after randomization until the study was terminated. The study was completed by 93% of the cohort, and average follow-up was 2.8 years (range 1.8-4.6).

The lifestyle intervention resulted in a 58% reduction in NIDDM compared with the placebo, and the lifestyle intervention was more effective than metformin. Metformin reduced the development of diabetes by 31%. Lifestyle intervention was beneficial regardless of ethnicity, age, BMI, or sex. The efficacy of lifestyle relative to metformin was greater in older persons and in those with lower BMI. The efficacy of metformin relative to placebo was greater in those with higher baseline fasting glucose and BMI.